The CRAC channel activator STIM1 binds and inhibits L-type voltage-gated calcium channels.

Journal: Science

Publication Year: 2010

Authors: Chan Young Park, Aleksandr Shcheglovitov, Ricardo Dolmetsch

PubMed link: 20929812

Funding Grants: Stanford CIRM Training Program

Public Summary:
Voltage- and store-operated calcium channels are the major routes of calcium entry in mammalian cells, but little is known about how cells coordinate the activity of these channels to generate coherent calcium signals. We found that STIM1 (stromal interaction molecule 1), the main activator of store operated calcium channels, directly suppresses depolarization-induced opening of the voltage-gated calcium channel CaV1.2. STIM1 binds to the C terminus of CaV1.2 through its calcium release–activated calcium activation domain, acutely inhibits gating, and causes long-term internalization of the channel from the membrane. This establishes a previously unknown function for STIM1 and provides a molecular mechanism to explain the reciprocal regulation of these two channels in cells.

Scientific Abstract:
Voltage- and store-operated calcium (Ca^{2+}) channels are the major routes of Ca^{2+} entry in mammalian cells, but little is known about how cells coordinate the activity of these channels to generate coherent calcium signals. We found that STIM1 (stromal interaction molecule 1), the main activator of store-operated Ca^{2+} channels, directly suppresses depolarization-induced opening of the voltage-gated Ca^{2+} channel Ca(V)1.2. STIM1 binds to the C terminus of Ca(V)1.2 through its Ca^{2+} release-activated Ca^{2+} activation domain, acutely inhibits gating, and causes long-term internalization of the channel from the membrane. This establishes a previously unknown function for STIM1 and provides a molecular mechanism to explain the reciprocal regulation of these two channels in cells.